

Hyperbaric oxygen therapy for patients with COVID-19

John Kirby

Dr Cannellotto and colleagues have published a prospective, multi-centred, open-label randomised controlled study of hyperbaric oxygen (HBO₂) as an adjuvant treatment for patients with COVID-19 who have severe hypoxemia. The study included 40 patients, 20 in the HBO₂ treatment arm and 20 in a control (no HBO₂) arm who were unable to achieve an oxygen saturation of 90% despite oxygen supplementation. In the current era—both in terms of well conducted research and especially given the COVID-19 pandemic—this is a deceptively difficult challenge to overcome. HBO research is often hobbled by preconceptions about its utility and the costs of performing it appropriately. I would also point out that this was done in Argentina even though the majority of patients with COVID-19, if not the majority of HBO₂ chambers themselves, lie outside of that country. This group of interested, committed clinicians were trying to improve the care of their patients with COVID-19 in a time of a pandemic and also managed to write up their work on behalf of all. Bravo.

The study by Cannellotto and colleagues¹ balanced many factors relating to COVID-19 so as to be maximally safe for the enrolled participants. The authors selected a very low treatment pressure, 1.45 ATA, and by doing so attempted to minimise any haemodynamic risks for the enrolled patients. Those less familiar with HBO₂ should know that 1.4 ATA is the minimum therapeutic level for clinical HBO₂ use in the USA² and lower therapeutic pressures have been proposed for other clinical conditions, but such low treatment pressures remain a subject for further study. As the applied pressure surrounding the body is increased, higher levels of tissue oxygenation are achieved, but other changes in tissue responses, whole body cardiovascular effects and host inflammatory responses also occur, and some provoke haemodynamic changes that can increase risk for patients.³ Researchers are attempting to determine what might be optimal pressures for the treatment of COVID-19 and other conditions.⁴

The authors also chose a more cost effective, lighter weight model of an HBO₂ chamber (Revitalair technology), which is not a completely rigid chamber and does not appear to go much above 1.4 ATA. This may have assisted in running the study at three sites. Presumably should HBO₂ be found to be more efficacious than previously assumed, lower cost, lighter chambers for HBO₂ delivery would allow more patients to access treatments.

The study was stopped after a preliminary analysis suggested that HBO₂ therapy was safe and those receiving it had faster times to reduced oxygen needs. This meant that the study only included 40 patients where originally it intended to include 80 patients, which potentially prevented observation of significant differences in long-term outcomes. I think it is notable that the authors stopped the study when they felt adequate safety had been demonstrated, even when continuing the study might have contributed to further statistically significant effects.

While the authors showed a clear benefit in terms of fewer days to improvement in oxygen requirements, it is important to recognise some aspects of recruitment that could suggest which patients this form of HBO₂ therapy might apply to. The authors excluded patients if they could not remain in a seated position for more than 2 hours, although online depictions of the use of Revitalair chambers seem to demonstrate patients being in semi-recumbent or beach chair positions. In addition, the participants needed to be able to tolerate being off oxygen for 5 min for assessment of their room air saturations. Although this was not stated as an inclusion criterion, the authors do not tell us if patients decompensated during this time and thus were not able to be included in the study. Both of these aspects could mean that the patients in the study were not necessarily representative of all patients admitted to hospital with COVID-19 who remained hypoxic on oxygen therapy. Also none of the patients received antivirals or monoclonal antibody preparations, which might also suggest less severe infection (unless these treatments were not available in the hospitals). What might have been useful would have been to obtain the clinical parameters of the patients with

COVID-19 who were in hospital at the time of the study to understand the spectrum of illness of the included patients.

One enrolment criterion was SpO₂ <90% despite oxygen supplementation. A wide variety of oxygen supplementation methods have been used due to clinical parameters and patients' tolerance of these methods. More details about the methods of oxygenation used in these patients would be helpful to interpret the study results. Perhaps with larger numbers, we could determine which oxygen therapies (or failure thereof) are associated with improvement with HBO₂ therapy.

Finally, it would be helpful to understand the time frames from presentation of symptoms to diagnosis to need for oxygen or hospitalisation to enrolment? Additionally, if patients receiving HBO₂ returned to normal oxygen levels more quickly, did this achieve any cost savings in terms of earlier discharges or conservation of overall oxygen use?

Nevertheless, the data from this study are consistent with other recent work involving HBO₂ therapy in patients with COVID-19. These studies have shown that patients begin treatment with very high respiratory rates and raised inflammatory markers, both of which seem to decrease with HBO₂.^{5,6} during and even after HBO therapy periods. HBO has a direct effect on oxygen absorption and its delivery to the body's tissues, and therefore increases oxygen saturations. The mechanism by which this treatment decreases inflammation is still being worked out.

The study failed to find changes in acute respiratory distress syndrome, mechanical ventilation or death, but this is probably because of the small numbers in the study, and the selection of possibly a less critical cohort of patients. Larger studies must start with smaller studies. Alternative therapies must be considered. Could five to seven 90min HBO treatments when amortised for each patient's treatment course compete with other advanced therapies, such as antiviral based therapies for costs, logistical feasibility, value and efficacy?

As we all look to improve our global capabilities to combat the effects of COVID-19, this study demonstrates the value of looking to make the most of available resources to properly evaluate novel treatment modalities such as a lower cost, portable, lower pressure HBO₂ to make a clinical impact on this pandemic.⁴

Funding The author has not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Correspondence to Dr John Kirby, Washington University in St Louis, St Louis, Missouri, USA; kirbyj@wustl.edu

Patient consent for publication Not applicable.

Ethics approval This study does not involve human participants.

Provenance and peer review Commissioned; internally peer reviewed.

This article is made freely available for use in accordance with BMJ's website terms and conditions for the duration of the covid-19 pandemic or until otherwise determined by BMJ. You may use, download and print the article for any lawful, non-commercial purpose (including text and data mining) provided that all copyright notices and trade marks are retained.

© Author(s) (or their employer(s)) 2021. No commercial re-use. See rights and permissions. Published by BMJ.

Handling editor Ellen J Weber



To cite Kirby J. *Emerg Med J* Epub ahead of print: [please include Day Month Year]. doi:10.1136/emered-2021-212015

Received 22 November 2021
Accepted 23 November 2021



► <http://dx.doi.org/10.1136/emered-2021-211253>
Emerg Med J 2021;**0**:1–2.
doi:10.1136/emered-2021-212015

REFERENCES

1 Cannellotto M, Duarte M, Keller G. Hyperbaric oxygen as an adjuvant treatment for patients with Covid-19 severe hypoxaemia: a randomized controlled trial.

Emerg Med J 2020 <https://clinicaltrials.gov/ct2/show/NCT04477954>

2 Moon R, ed. *UHMS Indications Manual*. 14th ed. West Palm Beach, FL: Best Publishing, 2019.

3 Camporesi EM. Side effects of hyperbaric oxygen therapy. *Undersea Hyperb Med* 2014;41:253–7.

4 UHMS position statement -Hybaric oxygen for Covid19 patients. Available: <https://www.uhms.org/images/Position-Statements/UHMS>

5 Thibodeaux K, Speyrer M, Raza A, et al. Hyperbaric oxygen therapy in preventing mechanical ventilation in COVID-19 patients: a retrospective case series. *J Wound Care* 2020;29:S4–8.

6 Gorenstein SA, Castellano ML, Slone ES, et al. Hyperbaric oxygen therapy for COVID-19 patients with respiratory distress: treated cases versus propensity-matched controls. *Undersea Hyperb Med* 2020;47:405–13.